REMARKS

Claims 1-17 are pending in this application. Claims 1-3, 7-12 and 14-17 have been withdrawn from consideration. Claims 1-3, 7-12 and 14-17 have been canceled. Claims 4-6 and 13 have been rejected. Claims 4-6 and 13 have been amended. No new matter has been added by these amendments to the claims. Applicant is respectfully requesting reconsideration in light of these amendments to the claims and the following remarks.

I. Restriction Requirement

The Restriction Requirement placing claims 1-3 (pertaining to agents the interact with nucleic acid sequences) into Group I, claims 1-3 ((pertaining to agents the interact with nucleic acid sequences) into Group II, claims 7-9 and 14 (drawn to agents) into Group III, claims 10-12 and 15 (drawn to a method for treating cancer comprising using an agent of claims 4, 5, 6 and 13) into Group IV, and claims 4-6 and 13 (drawn to a method for identifying agents that modulate the activity of BRCC or that inhibit the expression of BRCC36 or BRE protein) into Group V, claim 16 into Group VI, claim 17 (pertaining to levels of nucleic acids detected) into Group VII, and claim 17 pertaining to levels of protein detected) into Group VIII, has been deemed proper and made Final. Accordingly, Applicant is canceling claims 1-3, 7-12 and 14-17, reserving the right to file continuing applications on the canceled subject matter.

II. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claims 4-6 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner suggests that claims 4-6 are indefinite in recitation of BRCC because the term is defined in different ways at different places in the specification as filed. Applicant has amended claims 4-6 to recite that BRCC is a multi-protein complex that consists of a specific list of proteins, namely BRCA2, BRCA1, and RAD51, as well as one or more proteins selected from the group consisting of BRAD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. Support for this amendment to the claims can be found at page 17, lines 9-14 where these specific proteins are listed as being BRCC components, and at page 5, lines 15-19 where it is taught that the BRCC complex consists of a complex of BRCA2, BRCA1 and RAD51 as well as other proteins. In this way, the claims as amended are specifically defining BRCC in a way that is consistent with the specification as filed and meet the requirements of 35 U.S.C. 112, second paragraph. Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claims 4-6 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner suggests that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant are that the inventor, at the time the application was filed, had

possession of the claimed invention. The Examiner suggests that the term BRCC is not adequately defined in the specification and since test methods rely on contacting BRCC or cells containing BRCC with test agents, the claims are not adequately described. Applicants respectfully traverse this rejection.

As discussed supra, Applicant has amended the claims to recite that BRCC is a multi-protein complex that consists of a specific list of proteins, namely BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BRAD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. Support for this amendment to the claims can be found at page 17, lines 9-14 where these specific components are listed as being BRCC components, and at page 5, lines 15-19 where it is taught that the BRCC complex consists of a complex of BRCA2, BRCA1 and RAD51 as well as other proteins. In this way, the claims as amended are specifically defining BRCC in a way that is consistent with the specification as filed and meet the requirements of 35 U.S.C. 112, first paragraph. Withdrawal of this rejection is respectfully requested.

IV. Rejection of Claims Under 35 U.S.C. 102

Claim 13 has been rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (1995). The Examiner suggests that this reference discloses methods for detecting changes in BRE expression by UV irradiation and differentiating agents in cell expressing BRE and as such teaches the method of claim 13. Applicant respectfully traverses this rejection.

At the outset, in an earnest effort to advance the prosecution of this case, Applicant has amended claim 13 to

recite that the test agents of the method are one the types of agents listed in the specification as filed at page 24, lines 18-21, as being the preferred embodiments. There it states that preferred embodiments of the present invention provide "antisense, siRNA, or RNAi molecules or ribozymes targeted to nucleic acid sequences encoding BRCC36 or BRE".

Li et al. (1995) teaches the treatment of fibroblast cells with either UV light or 4-nitroquinolone-1-oxide. The treatment resulted in significant decreases in the levels of BRE mRNA detected in the cells. Nowhere does this paper teach or suggest treatment of any type of cell or tissue with antisense, siRNA, or RNAi molecules or ribozymes targeted to nucleic acid sequences encoding BRE, as now claimed. MPEP 2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as amended. Withdrawal of this rejection is therefore respectfully requested.

Claim 13 has been rejected under 35 U.S.C. 102(b) as being anticipated by Silverman et al. (U.S. Patent 6,331,396). The Examiner suggests that this patent discloses methods of detecting changes in BRCC36 gene expression due to interferon-alpha, interferon-beta, or interferon-gamma. Applicant respectfully traverses this rejection.

Silverman et al. (2001) teach the inhibition of expression of BRCC36 (also known as c6.1A) with treatment with interferon-alpha, interferon-beta, or interferon-gamma. Nowhere does this patent teach or suggest treatment of any type of cell or tissue with antisense, siRNA, or RNAi molecules or ribozymes targeted to nucleic acid sequences encoding BRCC36, as now claimed. MPEP

2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as amended. Withdrawal of this rejection is therefore respectfully requested.

Claim 4 has been rejected under 35 U.S.C. 102(b) as being anticipated by Hashizume et al. (2001). The Examiner suggests that this reference teaches exposing a BRCA1 and BARD1 to E2F1, cyclin B1 and CstF50 and then testing for an effect on ubiquitin E3 ligase activity. Applicants respectfully traverse this rejection.

At the outset, claim 4 has been amended as discussed *supra* to recite that the BRCC of the instant invention is a multi-protein complex that consists of a specific list of proteins, namely BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BARD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. Support for this amendment to the claims can be found at page 17, lines 9-14 where these specific proteins are listed as being BRCC components, and at page 5, lines 15-19 where it is taught that the BRCC complex consists of a complex of BRCA2, BRCA1 and RAD51 as well as other proteins.

Hashizume et al. (2001) teach that BARD1 association with BRCA1 potentiates the newly discovered ubiquitin E3 ligase activity of BRCA1 protein. Further, the paper teaches that E3F1, cyclin B1 and CstF50, compounds failed to stimulate Ub ligase activity. However, nowhere does this paper teach or suggest that these compounds modulate ubiquitin E3 ligase activity or ubiquitin hydrolase activity of a BRCC such as is defined in

amended claim 4, a BRCC that consists of BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BARD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. This list does not include a BRCC consisting of only BRCA1 and BRAD1 as taught in the cited reference. MPEP 2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as amended. Withdrawal of this rejection is therefore respectfully requested.

Claim 4 has been rejected under 35 U.S.C. 102(a) as being anticipated by Mallery et al. (2002). The Examiner suggests that the reference discloses a method comprising exposing BRCA1/BARD1 to BAP1, a ubiquitin hydrolase, to test for deubiquitylation of a polyubiquitylated form of BRCA1/BARD1. Applicant respectfully traverses this rejection.

As discussed *supra*, claim 4 has been amended to recite that the BRCC of the instant invention is a multi-protein complex that consists of a specific list of proteins, namely BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BARD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. Mallery et al. (2002) disclose that BRCA1 and BARD1 form a heterodimeric complex and that both proteins contain E3 ubiquitin ligase activity within their N-terminal zinc RING-finger domains. The paper provides data showing the dual E3 ubiquitin ligase activity of the human BRCA1/BARD1 complex. However, nowhere does this paper teach or suggest that these compounds modulate ubiquitin E3 ligase activity of a BRCC such as is defined in amended claim 4, a BRCC

that consists of BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BARD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. This list does not include a BRCC consisting of only BRCA1 and BRAD1 as taught in the cited reference. MPEP 2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as amended. Withdrawal of this rejection is therefore respectfully requested.

Claim 5 has been rejected under 35 U.S.C. 102(b) as being anticipated by Preisler et al. (1999), as evidenced by Vissac et al. (2002). The Examiner suggests that Preisler et al. (1999) discloses a method for identifying an agent that alters DNA repair in MCF-7 cells, while Vissic et al. (2002) provides evidence that MCF-7 cells express BRCA1 and BRCA2, and as such the paper of Preisler et al. (1999) tech a method of identifying an agent that modulates DNA repair activity of BRCC with a test agent and monitoring the ability of the agent to alter cell survival rates. Applicants respectfully disagree with the Examiner's conclusions regarding this prior art reference.

Priesler et al. (1999) describe the effects of treating cells, including MCF-7 cells, with a combination of paclitaxel and radiation. The specific effects being monitored are the genotoxicity of these agents as measured by the micronucleus assay. The micronucleus assay is a standard genotoxicity assay that measures the amount of DNA damage induced by a toxicant, such as paclitaxel and radiation. As discussed in any standard textbook of genotoxicity test methods, the objective is to

measure clastogenic activity of agents, where clastogenesis is defined as chromosome breakage (see for example page 569 of Hayes, A.W. 1994. *Principles and Methods of Toxicology,* 3rd edition, Raven Press: New York). Therefore, contrary to the Examiner's suggestion this paper does not teach a method of modulating DNA repair, as claimed specifically in claim 5. Instead, it is a method for detecting DNA damage. The micronucleus assay is also not a method for measuring cell survival rates as claimed in the instant invention (see claim 5). Instead, the assay measures the presence of micronuclei within cells. MPEP 2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as filed, which specify monitoring the ability to either alter cell survival rates in the presence of ionizing radiation or to alter homology-directed DNA repair. Withdrawal of this rejection is therefore respectfully requested.

Claim 5 has been rejected under 35 U.S.C. 102(b) as being anticipated by Pradier et al. (1999) as evidenced by Vissac et al. (2002). The Examiner suggests that this reference teaches a method for identifying an agent that alters radiation sensitivity in MCF-7 cells and that Vissic et al. (2002) provides evidence that MCF-7 cells express BRCA1 and BRCA2. Therefore, the Examiner suggests that this reference discloses a method of identifying an agent that modulates DNA repair activity of BRCC comprising contacting BRCC with a test agent and monitoring the ability of the agent to alter cell survival rates. Applicant respectfully traverses this rejection.

Applicant respectfully points out that contrary to the Examiner's suggestion, this paper does not measure DNA repair. Instead, it measures the survival of cells exposed to paclitaxel and radiation, where paclitaxel is shown to sensitize cancer cells to the effects of radiation. Pradier et al. 91999) teach that combining paclitaxel with radiation is an effective method for sensitizing cancer cells to the cell death induced by radiation. However, nowhere does this paper teach or suggest a method of identifying agents that modulate DNA repair activity of a BRCC such as is defined in amended claim 5, a BRCC that consists of BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BARD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. This list does not include a BRCC consisting of only BRCA1 and BRCA2 as taught in the cited reference. MPEP 2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as amended. Withdrawal of this rejection is therefore respectfully requested.

Claim 6 has been rejected under 35 U.S.C. 102(b) as being anticipated by Blagosklonny et al. (1995) as evidenced by Vissic et al. (2002) and Saramaki et al. (2006). The Examiner suggests that this reference teaches a method for identifying an agent that alters the expression of p21WAF1, which as evidenced by Saramaki et al. (2006) is encoded by a gene that contains a p53 response element. The Examiner suggests that Blagosklonny et al. (1995) teach the method in MCF-7 cells which are cells that express BRCA1 and BRCA2, as evidenced by Visic et al. (2002).

Thus, the Examiner suggests that this reference teaches a method of identifying an agent that modulates the transcriptional regulatory activity of BRCC comprising contacting a cell containing BRCC with a test agent and monitoring the ability of the agent to alter expression of a gene containing a p53 response element. Applicant respectfully traverses this rejection.

Blagosklonny et al. (1995) disclose that taxol treatment of MCF-7 cells induces p21WAF1 which requires c-raf-1 activity that is not strictly dependent on wild-type p53 activity. Although the other references teach that the p21WAF1 gene promoter is regulated by p53, and that the cells tested express BRCA1 and BRCA2, nowhere does this paper teach or suggest a method of identifying agents that modulate the transcriptional regulator activity of a BRCC such as is defined in amended claim 6, a BRCC that consists of BRCA2, BRCA1, and RAD51, as well as one or more of the proteins selected from the group consisting of BARD1, BRCC300, BRCC140, BRCC130, BRCA1 Δ11, BRCC80, BRE, and BRCC36. This list does not include a BRCC consisting of only BRCA1 and BRCA2 as taught in the cited references. MPEP 2131 states that in order to anticipate an invention the cited reference must teach each and every limitation of the claims. Accordingly, the reference cited fails to teach the limitations of the claims as amended. Withdrawal of this rejection is therefore respectfully requested.

V. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **April 16, 2007**

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